PRELIMINARY PROGRAM

ASBMB Fall Symposium
Subcellular Targeting of Signal Transduction Enzymes
October 11-14, 1996
Park City, Utah

October 11 (Friday)

Evening: ***Opening Lecture***

Tony Pawson, FRS
Samuel Lunenfeld Research Institute

October 12 (Saturday)

Morning: ***Compartmentalization of Multienzyme complexes***
Chair: John Scott, Vollum Institute, Oregon Health Sciences University

Invited speakers
Ann Marie Pendergast, Duke University
Beverly Errede, University of North Carolina

Afternoon: ***Poster sessions***

Special lecture: Susan Taylor, UCSD

Evening ***Targeting of kinases***
Chair: Susan Jaken, Alton Jones Cell Science Center

Invited speakers
G. Stanley McKnight, University of Washington
Daria Mochly-Rosen, Stanford University

October 13 (Sunday)

Morning: ***Structural Motifs for Subcellular Targeting***
Chair: Susan Taylor, University of California,San Diego

Invited speakers
Brian Hemmings, FMI, Basel
Stephen Sprang, University of Texas, Southwestern Medical Center

Afternoon: ***From the Membrane to the Nucleus***
Chair: Roger Tsien, University of California,San Diego.

Invited speakers
Lee Limbird, Vanderbilt University
Richard Goodman, Vollum Institute, Oregon Health Sciences University

October 14 (Monday)

Morning: ***Membrane Translocation***
Chair, Alexandra Newton, University of California,San Diego

Invited speakers
Jim Clarke, Genetics Institute
Carolyn Buser, SUNY Stonybrook
Claudia Kent, University of Michigan
Alan Aderem, University of Washington

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October 11-14, 1996
Subcellular Targeting of Signal Transduction Enzymes

Intracellular transduction of signals from the plasma membrane to specific subcellular compartments is a complex and highly regulated process that controls a myriad of essential cellular events. Perhaps the most graphic demonstration of how signal transduction pathways are essential to maintain cellular homeostasis is the overwhelming evidence that most transforming oncogenes encode signal transduction components such as low molecular weight G-proteins, protein kinases or phosphatases. Furthermore, it is becoming apparent that upwards of 20% of the genome encodes signal transduction components. Now that many of these genes have been identified, the challenge facing researchers is to figure out how these enzymes interface to control cellular events. Not surprisingly, regulation of signal transduction pathways is a sophisticated process that is achieved on many levels. A critical element in this process is the subcellular location of each signal transduction component [Newton 1995].

One emerging mechanism is that the subcellular distribution of several kinases and phosphatases is restricted by association with targeting proteins or subunits [Mochley-Rosen 1995]. A variation on this theme is the formation of kinase/phosphatase signaling complexes to modulate the phosphorylation state of specific target substrates [Faux and Scott 1996]. For example, the action of many tyrosine kinases (PTKs) and tyrosine phosphatases (PTPases) is coupled to downstream cytoplasmic enzymes through adapter proteins that contain SH2 and SH3 domains [Pawson 1995]. Modular proteins like Grb2, p85, IRS-1, Crk and Nck consist of a single SH2 domain that recognizes certain phosphotyrosyl residues on signaling enzymes, and two SH3 domains that bind to a PXXP motif on a separate set of target proteins including cytoskeletal components, enzymes involved in phospholipid metabolism or small molecular weight G-proteins [Pawson 1995]. Similarly, the targeting of many phospholipases, kinases, phosphatases and heterotrimeric G-proteins is mediated by specific membrane-targeting motifs such as the C2, pleckstrin homology and lipid-anchoring domains. Through these interactions signaling complexes are formed which generally emanate from receptor kinases or scaffold proteins and mediate cellular processes including growth factor signaling events, insulin action and immune cell function [Harrison and Errede 1995].

A flurry of recent advances from a variety of laboratories indicate that this is a prime time to evaluate the role of subcellular targeting in the regulation of signal transduction pathways. Accordingly, this meeting will focus on the proteins and structural motifs that function to target signal transduction components. The presentations will range from structural analysis of protein targeting motifs to the use of sophisticated functional assays and genetic techniques to identify novel targeting components. The symposium will open with a lecture from Dr. Tony Pawson, FRS, who has conducted many of the pioneering studies on src homology domains and the modular adapter proteins. The five scientific sessions will cover: compartmentalization of multienzyme complexes, targeting of kinases, structural motifs for subcellular targeting, signal transduction from the membrane to the nucleus, and membrane translocation. Each session will be chaired by individuals who have made seminal contributions to the field and will feature six speakers. The majority of the speakers will be selected from the abstracts. Participation of women and minorities will be encouraged.

In keeping with the spirit of the ASBMB Fall Symposia every effort will be made to encourage the participation of younger investigators, students and postdoctoral fellows. As part of this process, four of the speaking slots in each session will be filled by topics selected from the abstracts. There is no doubt that both of the organizers will positively discriminate toward young investigators as Drs. Newton and Scott were newcomers who benefited tremendously from the opportunity to participate in the 1992 ASBMB Fall Symposium on Protein Kinases and Phosphatases.

SATURDAY EVENING

Targeting of kinases
Chair: Dr. Susan Jaken, Alton Jones Cell Science Center

The goal of this session is to emphasize the recent progress on the subcellular targeting of protein kinases through association with anchoring proteins and targeting subunits. The invited speakers will be Dr. G. Stanley McKnight, University of Washington and Dr. Daria Mochley-Rosen, Stanford University. Potential laboratories that may contribute to the session include those of Rubin, Colbran, Cohen, DePaoli, Aderem and Gallatin.

SUNDAY MORNING

Structural Motifs for Subcellular Targeting
Chair: Dr. Susan Taylor, University of California, San Diego

This session will focus on the structural biology of subcellular targeting motifs. This will include lectures on structural analysis of C2, SH2, and pleckstrin homology domains. The invited speakers will include Dr. Steve Sprang (C2 domain), PH domain (from a company Ask ACN). SH2 domain (Ariade). Potential laboratories that may contribute to the session include those of Kuryan, Jennings and ICOS corporation.

SUNDAY AFTERNOON

From the Membrane to the Nucleus
Chair: Dr. Roger Tsien, University of California, San Diego.

The concept of this session is to provide a session which emphasizes the contribution of subcellular targeting on the function of various transduction molecules. This will include discussion of basolateral vs. apical targeting of G-protein linked receptors by Dr. Lee Limbird, Vanberbilt University to the formation of the nuclear CREB transcription complex through association with CREB-binding protein from Dr. Richard Goodman, Vollum Institute. Potential laboratories that may contribute to the session include those of Hamm, Morrison and Karin.

MONDAY MORNING

Membrane Translocation
Chair, Dr. Alexandra Newton, University of California, San Diego

The goal of this session is to discuss the role of membrane translocation in signal transduction events and the function of targeting sequences that localize signaling enzymes close to membranes and cytoskeleton. The invited speakers will be Dr. Jim Clarke, (Genetics Institute) and Dr. Stuart McLaughlin, SUNY Stony Brook, Dr. Claudia Kent, University of Michigan, and Dr. Brian Hemmings, FMI Basel. Potential laboratories that may contribute to the session include those of Lefcowitz, Aderem, Nairn, and Valee.